

FIG. 1

```

1  agttgagtcgcaatagtggtggaacttca aatgcccttactgtccggaacaaccacca ttgccagggtgtgcaggccagatttgtta
91  atttgtgaaaagtggaaaaatttattccg ctatgcctaaccgaagagcccgcaagaaga ggcggacagaagacttttccagctcttcgg
181 catctgaaaacgatagtgactccgagagcg tgaccagtgtagcaggaagagcagccggatg cgcccgaaacatacacaatagatggcctgg
271 acacgcaagaggtgtctgacagcacacagg tgagactccaacagctgaacgcagacaggt tggccagcatagagcaaacgctttcaggca
361 acctcaactggacataaacgcagtagcgcc agatagatgatgtgcgtgagcagctgcaga acgagtatttgaagaaattgctgtgcacat
451 attctgaggacctggatgctgctgctgaga aaaccgatttcaaggaaaactcactcaaaa ccctcgcccgctcttctcaagagagcgga
541 acatatitgatgatggaactctcaagtcgc tagttgagtgatgtatatgataatgtctaa ttttaattttcatcagtggtgcaagatctgg
631 gcttagccgttctaaatggtatattcagggc tgtgcaagccacattttaaattaccctatc gggttttaatttctattgttagaaattagg
721 atctacatagaggtagagtgagcaacagaa cattgtttgctatccgggcccctccgactgg aacgtcttaccttcagctactatttattca
811 gaaaaaagagtgcattttcatctatcaagg tctcaagtgctgaatcaaatcactagtat tttttccgagactaaaaaaagttagacaca

901  ATGAAAGTTGCTACACTGTTTTCTTGGCT TCGAGTGTCTGTGTCTGGGAGACCCACAG TTCGTGAAACTGGAGGCTCTGTTCTTCGG
① M K V A T I F F L A S S V C V I G D P Q F V K L E A S V L R
991  GGATCCACTTACAAGGATTCAGAGAAGGGG GCCAAGCCGTTTCATGTTGGAAAAGAGGGCT GATGACGGCTCGGTACGATGGAATTCAG
G S T Y K D S Q K G A K P F M L E K R A D D G S V T F N P S
1081 AACGCCAGTCTTTCTACCAAGTCGAGATC GAGATAGGATCTGATAAGCAGAAGGTGGGG GTTTTGATTGATACCGGTTCTCGGACTTG
N A Q S F Y Q V E I E I G S D K Q K V G V L I D T G S S D L
1171 TGGGTGATGAACTCGAATAACTCTTACTGT TCGTCTTCCAGCACTAAAAAATTGAAACGG GACGGACCGGCGATGCGCTACAAAAAGGA
W V M N S N N S Y C S S S T A K K L K R D G P A D A Q K G
1260 CGCGATCTTTCGACCTGTACAATTTCAAC TCTCCAAACGAAGACAACATGCAAAAGGA TTCTTGGGTGGCTGGGAGACTTGACCACA
R D L S D L Y N F N S P N E D N N A K G F L G G W G D L T T
1351 GTAGAGACTGCAACCCAGGATGAGACACAG ACGGCTCTCGTGGCAGGCCACCGTGGAC TGCTCGCTATACGGAACGTTCAATCCTTCA
V E T A T Q D E T Q T A L A Q A T V D C S L Y G T F N P S
1441 ACGTCCAATTCGTTCCACAACAACGGCAAC ACATTTGAGATTTCTGACGGGACCGCACT TTTGCCCGTGGAACTGGGGCTACGATGAT
T S N S F H N N G T T F E I S Y A D R T F A R G T W G Y D D
1531 GTCATTTCAATGGTGTACGGTTAAGCAT CTCTCGTTGGCGTGGCAGATGAAACAGAT TCTTCGACTGGTGTGTTTGGTATCGGATTG
V T F N G V T V N D L S L A V A D E T D S S T G V F G L
1621 AGGGAATTGGAACACACATACTCAGGAGGC GGACCACAGCATTACATCTACGACAACCTA CCTTTCAAAATGGTCGACCGGAGTATC
R E L E T T Y S G G G P Q H Y I Y D N L P F K M V D Q G L I
1711 AATAGAGCGCCTATTCCGCTACCTGAAC TCAACTGAGTCCAGCACTGCCTCGATCCTC TTCGGTGCGGTTGACCAAGCAAATATACC
N R A A Y S V Y L N S T E S S T A S I L F G A V D Q S K Y T
1801 GGAAGTCTTGGCTTCTTCTATCATCAAC ACGGCTGCTTCTACGGTTACCAAAAGCCT CTAAGGCTCCAATCACCTGTCTGCATT
G S L G L L P I I N T A A S Y G Y Q K P L R L Q I T L S A I
1891 ACGGTGAGGACTCCAGAGGACAGCAAGCA AGCATTGGTTGAGGAGCTGCTGCTGCATT CTTGATACCGGAACGACTTTGACGTATGCT
T V S D S R G Q A S I G S G A A A A L L D T G T F N P S
1981 CCAAGCGAGATTGTCGAGAACTTGCTGAA ACCCTAGGCTTCGACTACAGCAGCTCTGTC GGGGCTACGTGGCAAGATGCAAGGACGTT
P S E I V E K L A E T L G F D Y S S S V G A Y V A R C R D V
2071 GATAGCTACGCTGTCAACTTCGACTTCAG GGTAAAGTGATTGAAGCTCCTTGAGTTCC TTCCTGATTGCTCTGCAACCAACTCCGGA
D S Y A V N F D F Q G K V I E A P L S S F L I A L Q T N S G
2161 GAAGTTTCTCTACTGCGCATTGGGTATT TTCTCTCTGGAGACGAATCCTTCACGCTC GCGGACTTTCTCTGCGAAACGCTACTTT
E V S S Y C A L G I F S S G D E S F T L G D T F L R N A Y F
2251 GTGGTGACCTCGAGGGATATCAAAATCGCT ATAGCTAACGTGAACCTGAATCCTGGAGCC GAGCAAATTGAGGTCTCTCAGGCAACTCC
V A D L E G Y Q I A I A N V N L N P G A E Q I E V I S G N S
2341 ATTCTTCTGCTTCTGTCGTTTCCGATTAC TCCAATACCTGGGGCGCTCTGCCACCGCT TTGGACTGACAGGCTACTACTCTGGGA
I P S A S S V S D Y S N T W G A S A T A L D T D R P T T L G
2431 TCTGTGACTGCTGTGGCGATGAAAGAGTG ACCTCGACCAAGAAGGTTTCGAGTGTGAAG ACAAGCACTTCGTCGGGTCCGGGTCCACT
S V T A V G D E R V T S T K K V S S V K T S T S S G T
2521 TCGGAGTCGTCTACGTCCAGTTCGATTCC AGCAATGGCCCAAGGACAGTAGGCTTTAGT TTGTGTGCCGTTTGTGCGCATTCTTGATT
S E S S T S S S H S ② S N G P R T V G E S I C A V I C A F I I
2611 TCTATACTAGTTGTTGCTagatctgaagt tctaaggggctttagcttcatattatgatt ttttttatttggaccgctcgaattgttt
S I I V V C
2701 ttccgacgggtctacttttaagctgcaaga tctcgittagcgctgtttatttctcgttcg tttagtgacaaaaaacagaaaaaaact
2791 ataaaaagcgggtatataacctttatatttt gataaacatgagcagcgaaattagctagc accaaaggatttacgagaaggacaagggtt
2881 cgccaaggctctgcatggcaaggagcgccgc gagcgctacaggaatgagtgcttgggtgaa gaaggacaaggaagctcaaaagtcgcgat
2971 ggaaggatatttcaagcactgggacgggaa aaccgacgagggactgaaaagtcgagact cgaggactactcgagctcaccgaagcacta
3061 ctacaacctggtagcggatttctacpagta tggatggggatcctcgttccacttttccag atactacaaggagagccatttagacaagc
3151 t

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FIG. 2

HpYPS1 : MKVATLFFFLASSV----CVLG-----DPQFVKLEASVLRGSTYKDSQKGAKPFMLEKRADDG : 53
ScYPS1 : MKLKTVRSAVLSSLFASQVLGKIIPAANKRDDDSNKFVKLPFFKLYGDSLENGSDKKPEVRLLKRADG : 70
ScYPS2 : MKLSVLTFVVDALLVCSSIVDAGV--TDFPSLPSNENVVVKMNFQKKYGSSFENALDDTKGRTRLMTRDD : 68
ScYPS3 : MKLQLAAVATLAVL-TSPAFAGRVLP-----DGRVVKLPFTKK-----KNGDNGELSKRSNG : 50

HpYPS1 : SVTMEQNAQSFYQVEIEIGSDKQKVGVLIDTGSSOLWVMNSNNSYCSSSSTKKLKR---DGPADALQKG : 120
ScYPS1 : YEEIITNQQSFYSVDLEVGTPPONVTVLVDTGSSDLWIMGSDNPYCSSNSMGSSRRRVIDKRDDSSSGG : 140
ScYPS2 : YELVELTNQNSFYSVLELDIGTPPOKVTVLVDTGSSDLWVTGSDNPYCSTKKKDTTGSSSF--KQVKNDALA : 136
ScYPS3 : BEKFVLANEQSFYSVLELAIGTFSQNLTVLLDTGSDLVWVPGKGNPYCGS----- : 99

HpYPS1 : RDLSDLYNFNSPNEDNNAGFLGGWGLTTTETATQDETQTALAAQATVDCSLYGTENPSTNSFHNNGT : 190
ScYPS1 : SLINDINPFGWLTGTGSAIGP-----TATGLGGSGTATQSVPAEATMDCQYGTSTSGSSSTFRSNT : 205
ScYPS2 : SVVESV--F-----TEISY-----DTTITVTEATATFDTASTSGLIDCATYGTENTSKSSTFNSNT : 192
ScYPS3 : -----VMDCCQYGVEDKTKSSTFRANKS : 122

HpYPS1 : T-EEISYADRTFARGTWGYDDVTFNQVTVNDLSLAVADETDSSTGVFGIGLRELETTYSGG---GPFQHY : 255
ScYPS1 : Y-ESISYGDGTFASGTFGTVDVLDLSDNMTGLSFAVANETNSTMGVGGIGLPELEVITYSGSTASHSGKAY : 274
ScYPS2 : E-ESIAYGDTTFASGTWGEDQLSLNDNMTGLSFAVANETNSTVGVLGIGLPGLESTYSGVSLSSVQKSY : 261
ScYPS3 : SPEYAAVGDGTYYAGTFGQDKLYNEVLDLSLFAVANESNSTFGVLGIGLSTLEVITYSGKVAIMDKRSY : 192

HpYPS1 : IYDNLPFKMVDQGLINRAAYSVYLNSTESSTASILFGAVDQSKYTGSGLPLPIINTAASYGYQKPLRLQI : 325
ScYPS1 : KYDNFPFVLKNSGAIKSNSTYSLYLNDSADAMEGTILFGAVDHSKYTGTLTIPIVNTLSAGSSSPIQFDV : 344
ScYPS2 : TYNNFPMVLKNSGVIKSTAYSLFANDSDSKEGTILFGAVDHCKYAGDLITPIINTLQHRGYKDPICFQV : 331
ScYPS3 : EYDNFPFLFKESGAIDATAYSLFLNDESQSSGSILFGAVDHSKYEGOLYTTPLVNLKYSQYQHPYAFDV : 262

HpYPS1 : TISAITYVSDSRGQQ--ASIGSGAAAAALDTGTLTYAPSEIVEKLAETLGFDYSSSVGAYVARCRDV--D : 391
ScYPS1 : TINGIGISDSGSSNK--TLTTTKIPALSDSGTTLTYLPQTVMIAETELGAQYSSRIGYVLDCCPSD--D : 410
ScYPS2 : TLQGLGTSKQKEDNLTTLTTTKIPVLLDSGTTISYMPTELKMLADQVCATYSSAYGYIMDCIKEMEE : 401
ScYPS3 : TLQGLGL---QTDKRNITLTTLTKLPALLDSGTTLTYPQAVALLAKSLNASYSKTLGYEYTCPSD-DN : 328

HpYPS1 : SYAVNFDFFGQKVEAPLSSFLHALQTNSEGEVSSYCALGIFS-SGDESFTLGDTEFLRNAYFVADLEGYQIA : 460
ScYPS1 : SMEIVDFDGGGFHINAPLSSFLSTGT---T-----CLGIIPTSDDTGTILGDSFLTNAYVVDLENLEIS : 473
ScYPS2 : ESSIIIDFFGGFYLSNWLSDFOVTDNRNI---CILEGIAPQSDPT-IILGDNFLANTYVVDLDNMEIS : 466
ScYPS3 : KTSVAEFDGGRINAPLSDFTVQTSV--GT---CVLAIIPQAGNATAILGDSFLRNAYVVDLDNTEIS : 392

HpYPS1 : IANVNLPNGAPQIEVISGNSIPSASSVSDYNTWGSATALDTRPTTLGSVTAVG-----DERVTSTKK : 525
ScYPS1 : MAQARYNTTSENIEIITS-SVPSAVKAPGYNTWSTASIVTGGNIFTVNSSQTASF----- : 529
ScYPS2 : MAQANFSDDGTYEIIIES-AVPSALKAPGYSTWSTYESIVSGGNMFSTAANSSISYFASSTSHSATSSSS : 535
ScYPS3 : LAQAKYGTGKENVEVIRK-TVPSAIRAPSYNNTWSNYASATSGGNIFT-----VRTFNGTS-TATTRS : 455

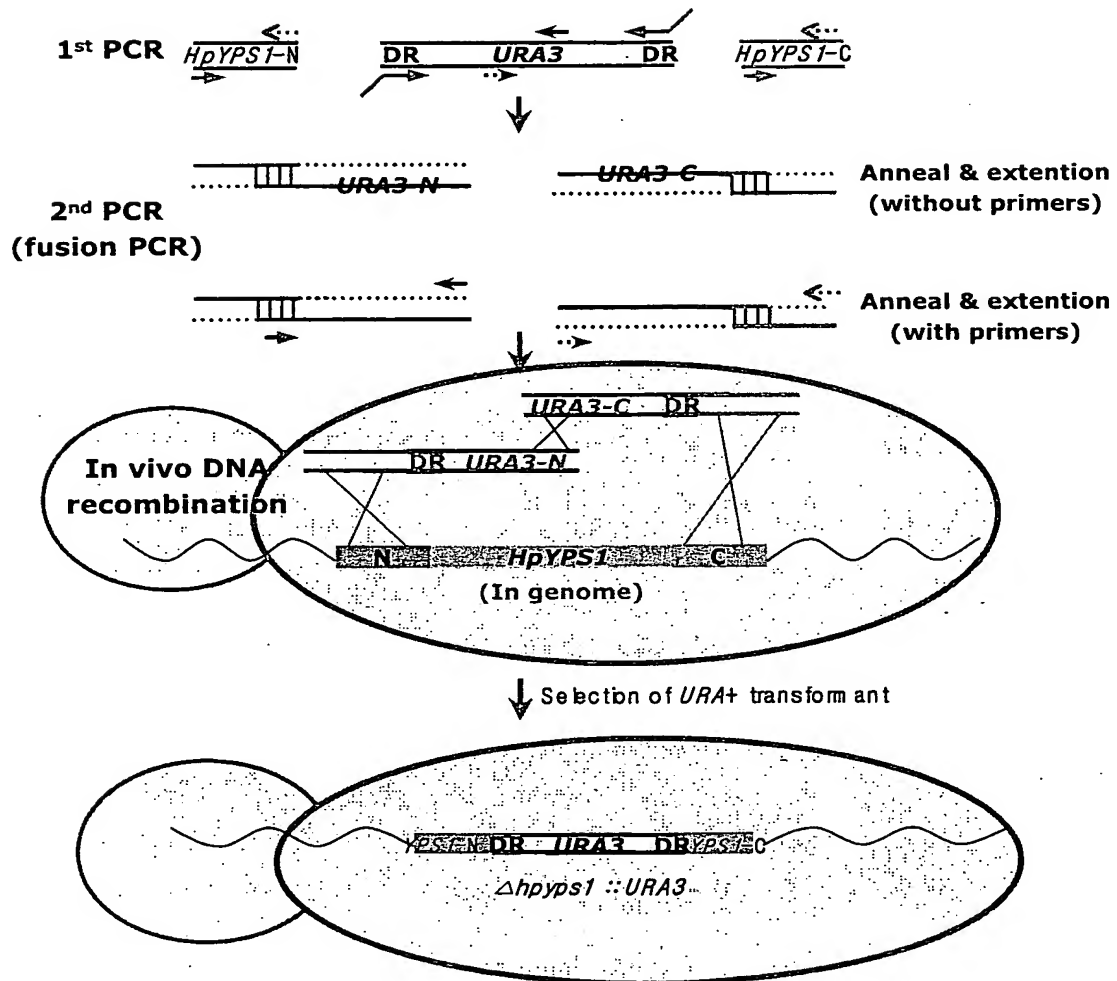
HpYPS1 : VSSVKTSTSSGSGSTSESSTSSSHS-----SNGPRTVGFSLCAVLCAFLISILV----- : 574
ScYPS1 : -----SGNLTTSTASATSTSS-----KRNVCDEHIVPSLPLTLISLLFA----- : 567
ScYPS2 : SKGQKTQTSTAALSISKSTSSSTGMLSPSTSSSPRKZNGCHNLNPPFFARFITAIFH----- : 594
ScYPS3 : TTTKKTNSTT---TAKSTHKKRALQRAATNSASSIRSTLGLLLVPSLL--LSVFFSPRHSAGSIISN : 519

HpYPS1 : -VC- : 576
ScYPS1 : --FI : 569
ScYPS2 : --HI : 596
ScYPS3 : PVYG : 523

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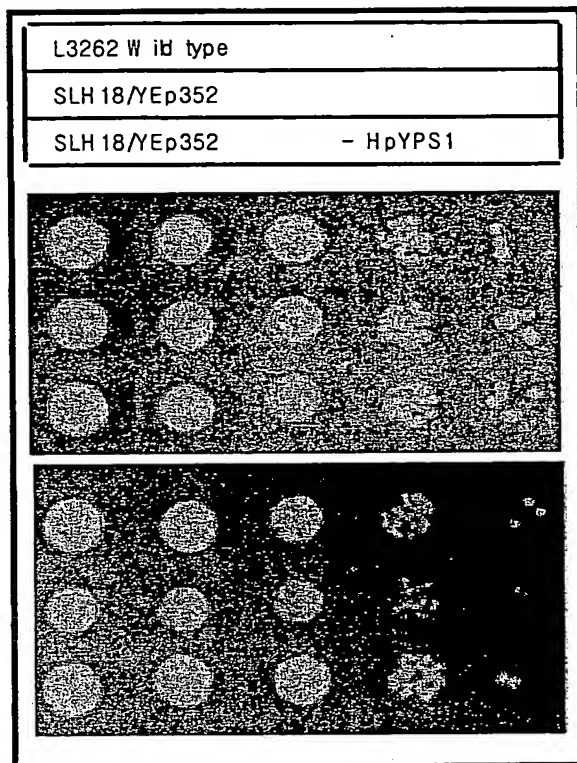
FIG. 3



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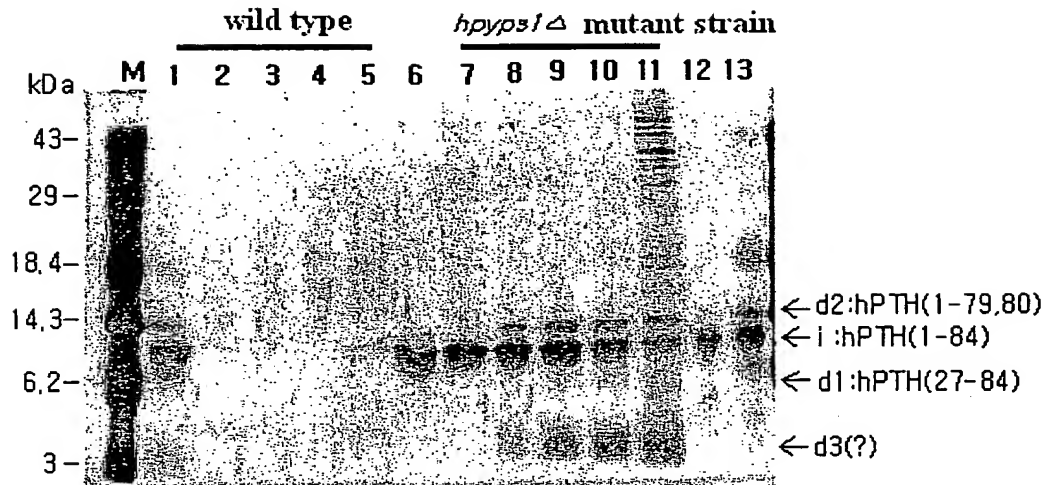
FIG. 4



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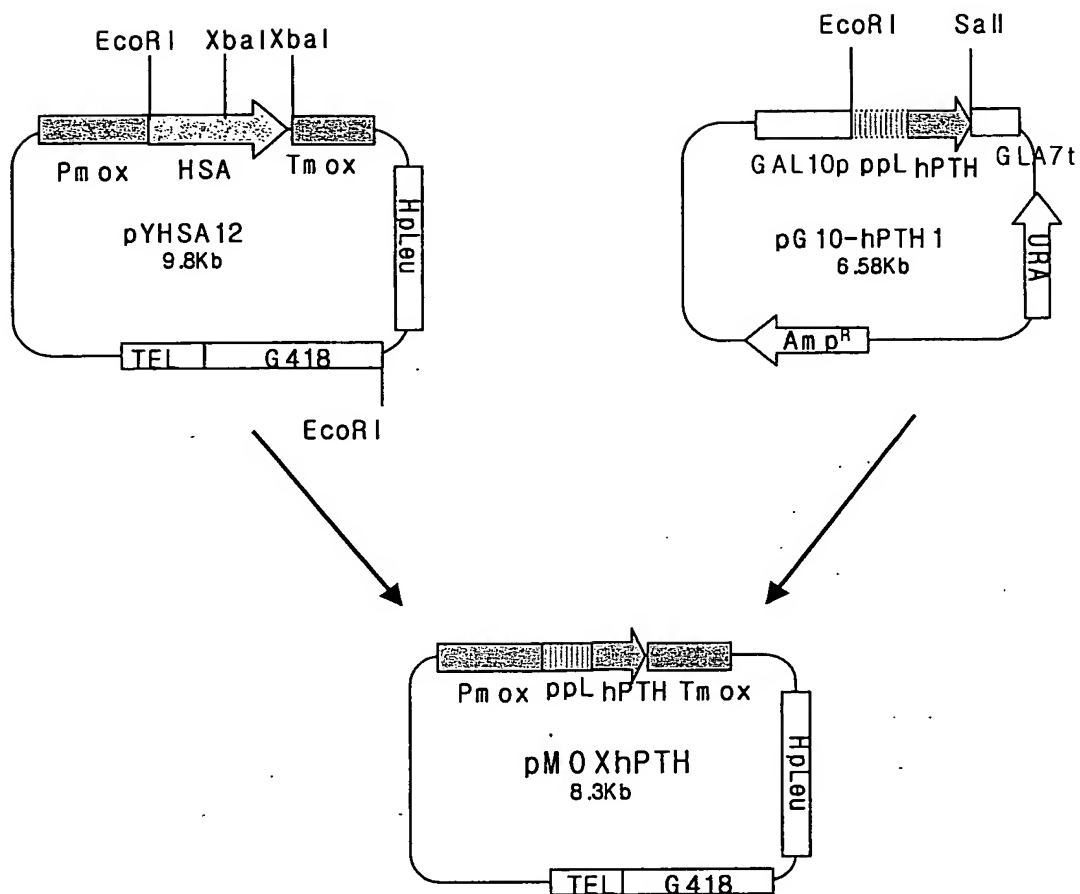
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FIG. 5

**Lane M: Molecular marker**

- 1: wild type, 0-h reaction
- 2: wild type, 2-h reaction
- 3: wild type, 4-h reaction
- 4: wild type, 6-h reaction
- 5: wild type, 24-h reaction
- 6: distilled water + hPTH, 0-h reaction
- 7: mutant strain, 0-h reaction
- 8: mutant strain, 2-h reaction
- 9: mutant strain, 4-h reaction
- 10: mutant strain, 6-h reaction
- 11: mutant strain, 24-h reaction
- 12: hPTH 100 ng
- 13: hPTH 200 ng

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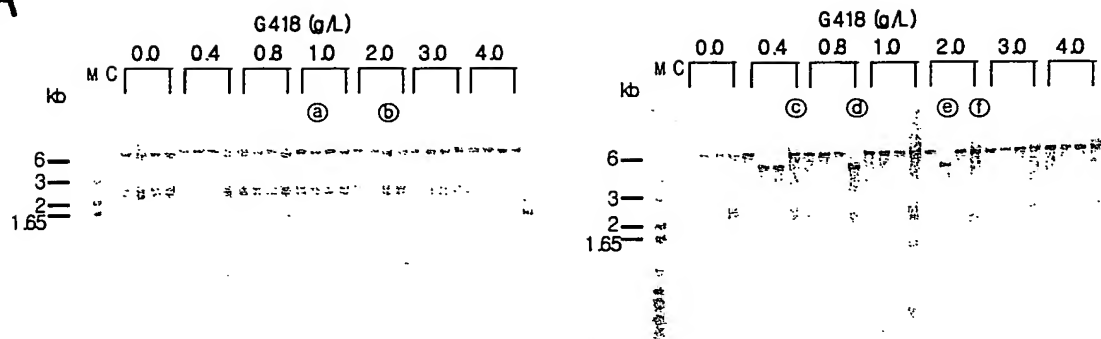
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FIG. 6

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FIG. 7

A

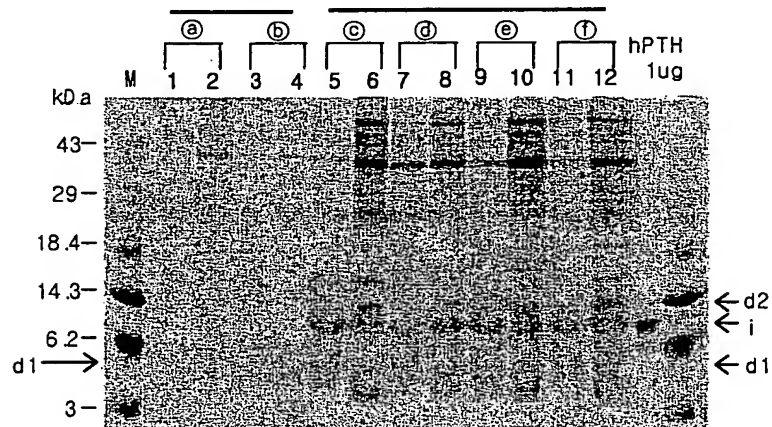


Transformants of wild type

Transformants of *hpypl* Δ mutant strain

B

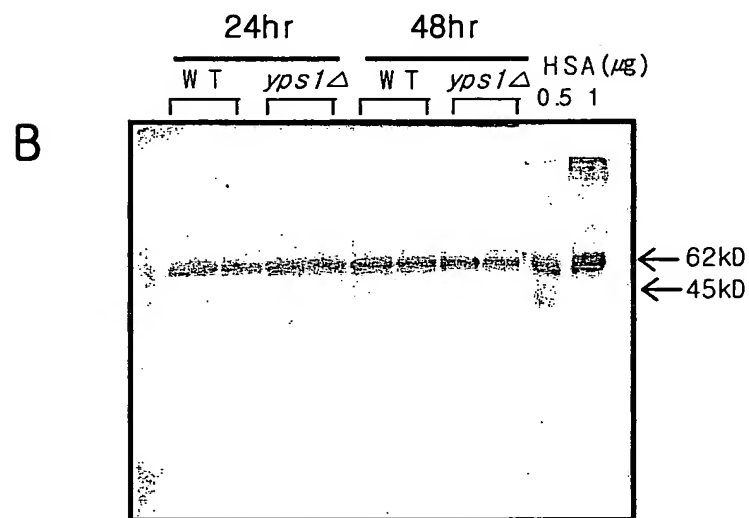
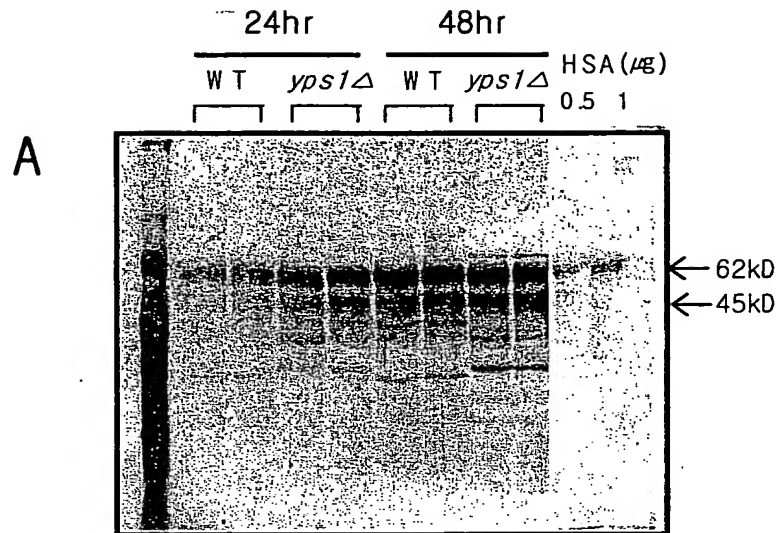
Yeast culture supernatants of wild type Yeast culture supernatants of *hpypl* Δ mutant strain



Lane 1, 3, 5, 7, 9, 11 : 12hr after initiation of the cultivation
 Lane 2, 4, 6, 8, 10, 12 : 24hr after initiation of the cultivation

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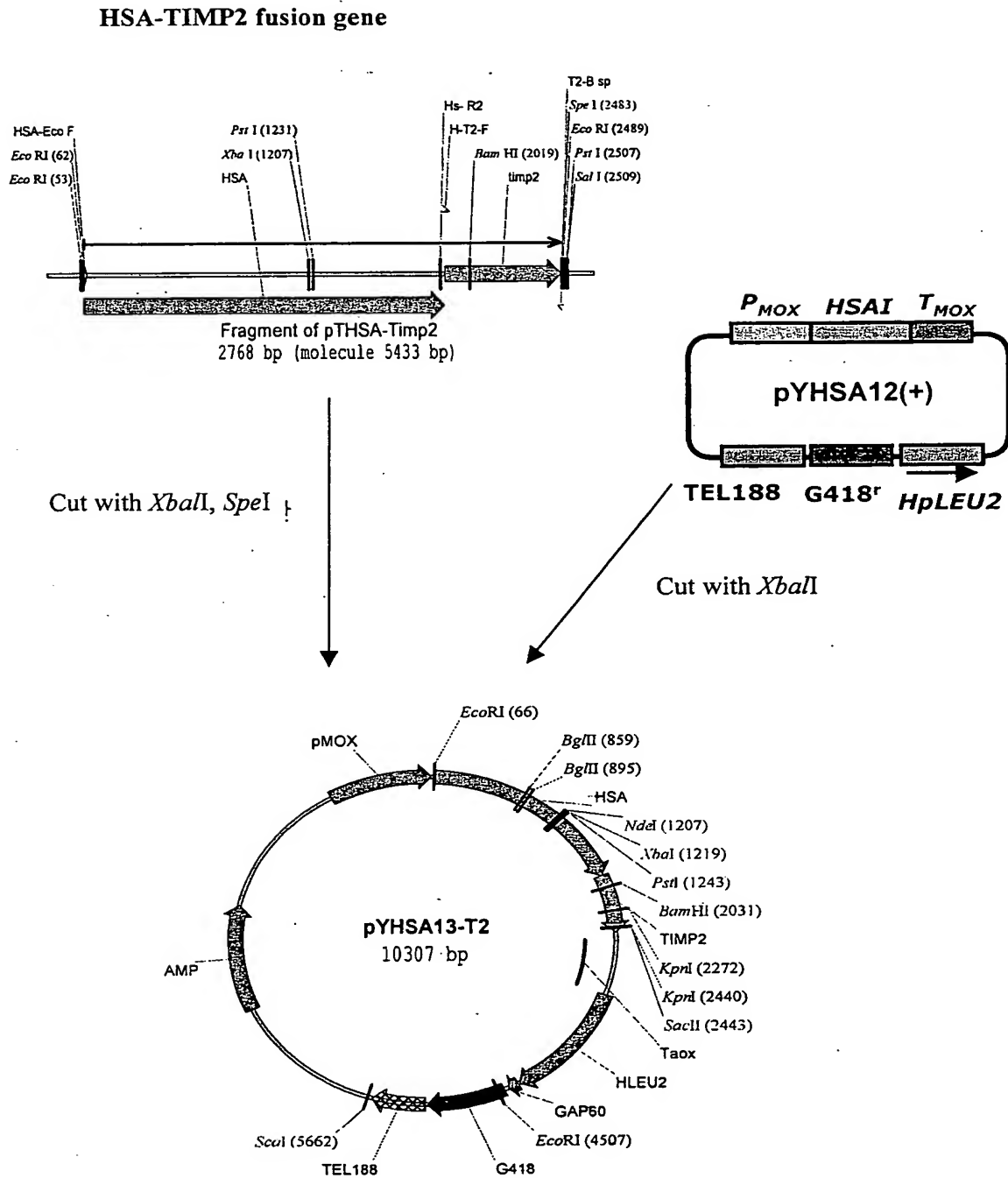
FIG. 8



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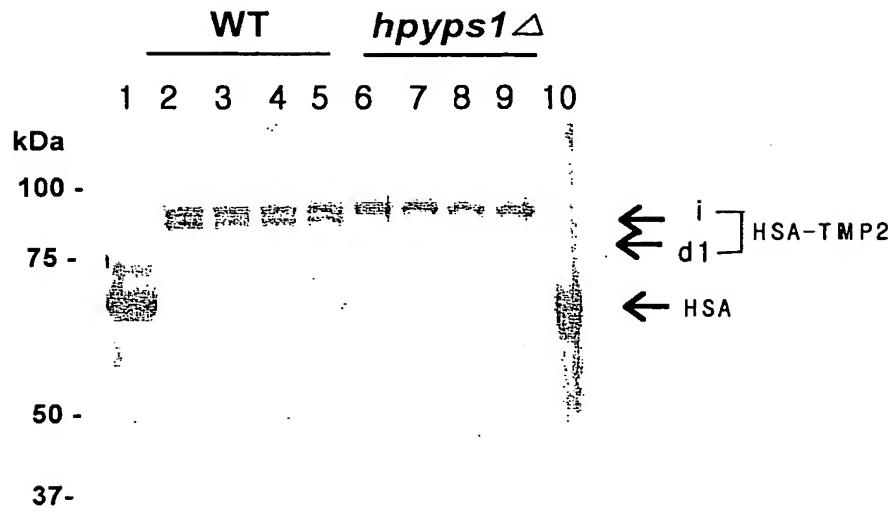
FIG. 9



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FIG. 10



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